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EXAMINER

WILDER, C

ART UNIT

PAPER NUMBER

1655

DATE MAILED:

08/07/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/402,260

Applicant(s)

Kawashima et al.

Examiner

CB Wilder

Art Unit

1655



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 30, 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 4-17, 21, and 23 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-17, 21, and 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☒ All b) ☐ Some* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 20) ☐ Other: _____

Art Unit: 1655

FINAL ACTION

1. Applicant's amendment filed 5/30/01 in Paper No. 15 is acknowledged. claims 1, 14, 17, and 21 has been amended. Claims 1, 2, 4-17, 21, and 23 are pending. The amendments and arguments have been thoroughly reviewed and considered but they are not found persuasive for the reasons discussed below.

This Action is made Final.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The claim rejection under 35 U.S.C. 112 second paragraph drawn to claims 1, 2, 4-17 as being indefinite is withdrawn in view of Applicant's arguments. The prior art rejection under 35 U.S.C. 102(b) directed to claims 1, 2, 4-13, 16 as being anticipated by Dover et al. is maintained. The prior art rejection under 35 U.S.C. 103(a) directed to claims 15, 17, 21 and 23 as being unpatentable over Dover et al. in view of Lewin is maintained.

Claim Rejections - 35 USC § 102(b)

4. Claims 1, 2, 4-13 and 16 rejected under 35 U.S.C. 102(b) as being anticipated by Dower et al. (5,547,839, Aug. 20, 1996). Regarding claims 1 and 2, Dower et al. teach a method for sequencing nucleic acid molecules, comprising the steps of: (a) providing at multiple locations, a

Art Unit: 1655

plurality of nucleic acid molecules wherein the plurality of nucleic acid molecules are single stranded or doubled stranded, (col. 14, lines 41 and 42) and have the same sequence as one another (col. 7, lines 58-63) and are able to hybridize to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase, providing each location with a nucleic acid polymerase and a given labeled nucleotide under conditions that allow extension of the primer if a complementary base or if a plurality of bases is present at the appropriate position in the nucleic acid molecules; detecting whether or not said labeled nucleotide has been used for primer extension at each location by determining whether or not the label present on said nucleotide has been incorporated into extended primers and if said nucleotide have been used in primer extension the step further include detecting the nucleotides used per extended primer. Dower et al. also teach wherein the primer extension step comprising multiple labels is repeated and whereby the sequence of the nucleic acid molecule is obtained by referencing to the signal depicted at each location and the identification of of nucleotides used in the primer extension at each location (col. 2, line 66 to col. 4, line 43, *See also col. 23, line 15 to col. 26, line 27*). Additionally Dover et al. disclose wherein the target nucleic acid can be converted into its complementary sequence (col. 14, lines 38-44).

Regarding claim 4, the washing step to remove excess nucleotides is inherent in the primer extension reaction for sequencing the nucleic acid molecules, as this step is routinely practiced in methods of primer extension to alleviate non-specific background noise and increase specificity of detection.

Art Unit: 1655

Regarding claim 5, Dower et al. teach wherein the detection step further comprise the use of absorption or emission spectrometry (col. 12, lines 6-67).

Regarding claim 6, Dower et al. teach wherein both the nucleic acid molecule and primers are immobilized (col. 28, claim 1).

Regarding claims 7-9, Dower et al. teach wherein the method is capable of sequencing hundreds, thousands or even millions of nucleic acid molecules simultaneously wherein the nucleic acid molecules have different sequences (col. 2, line 66-67 to col. 3, lines 1-12) and are sequence at 10 or more different locations such as in e.g. well of a microtiter dish (col. 10, lines 9-30).

Regarding claims 10-13, Dower et al. teach wherein four different nucleotides comprising dATP, dTTP, dGTP and dCTP in labeled form are used in the primer extension reaction (col. 27, line 53) and wherein the four different nucleotides are used in predetermined order in repeated cycles (col. 2, line 66 to col. 4, line 43). Dower et al. additionally teach that the target may be DNA or RNA. Therefore the use of the UTP instead of TTP is inherent in the teaching of Dower et al as this nucleotide along with ATP, GTP and CTP in labeled form would be used in primer extension of RNA nucleic acid molecules.

Regarding claims 16, Dower teach wherein one nucleic acid molecule is provided at each of the locations (col. 10, lines 14-21).

In view of the foregoing, the claimed invention of claims 1, 2, 4-13 and 16 are anticipated by the reference of Dower et al.

Art Unit: 1655

5. Applicant's amendment filed in Paper No. 15 has been thoroughly reviewed and considered but are not found persuasive for the reasons that follows. Applicant traverses the rejection on the following grounds: Applicant argues that "Dower repeatedly teaches that the removal of a label from a nucleotide used in primer extension is need before adding a further labeled nucleotide, whereas in contrast, with the present invention, whereby a plurality of labels are incorporated in a growing strand by primer translation (or nick translation), the need to remove labels is avoided. Applicant argues that such feature is reflected in step (c) of independent claims 1 and 17. Applicant's cites a passage from page 6 of the specification and argues that Dower by contrast to the instant invention do not teach a sequencing scheme in which each of the extended primers comprises a plurality of labels. Applicant further argues that the Dower et al. scheme requires removal of the label after each extension cycle. Applicant argues the importance of removal of the label is stressed throughout Dower et al. including in the various figures. Finally Applicant concludes that Dower et al. do not teach the presently claimed methods and withdrawal of the instant rejection is respectfully requested.

6. The arguments have been considered but they are not found persuasive for the reasons that follows: First, the courts have established that "during patent examination the pending claims must be interpreted as broadly as their terms reasonable allow" *In re Zletz*, 893 f. 2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). In this case, the open language ("comprising") of the claims suggest other method steps and/or reagents as being encompassed in the instant invention. Therefore the particular embodiment (removal of labels) of Dover et al. as Applicant argues is encompassed in the instant invention as written. Furthermore, the limitation Applicant argues wherein the "removal

Art Unit: 1655

of labels is avoided” is not recited in the rejected claims. There is no indication from the claims as written that the method steps of the instant invention indeed avoids removal of labels. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In view of the foregoing, the rejections under 35 U.S.C. 102(b) is maintained.

Claim Rejections - 35 USC § 103

7. Claims 15, 17, 21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al. in view of Lewin B, (Genes IV, Oxford University Press, New York, December 1990). Regarding claims 15 and 23, Dower et al. teach a method of sequencing nucleic acid molecules at multiple locations wherein the molecules are single stranded or double stranded having the same sequence or different sequences and wherein the method comprise a number steps such that primer extension is used to detect the sequence of the nucleic acid molecules. The sequencing method of Dower et al. differ from that of the claimed invention in that Dower et al. do not expressly teach wherein double stranded nucleic acid molecules having nicks are provided at the multiple locations. Lewin teaches a general method for providing nicks into double stranded nucleic acid molecules by nick translation. Lewin teaches that the method of nick translation for providing nicks into a double stranded nucleic acid molecule is of great practical use for introducing labeled nucleotides into DNA (page 347, col. 2, 5th full paragraph). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have provided double stranded nucleic

Art Unit: 1655

acid molecules comprising nicks as taught by Lewin in the primer extension sequencing method of Dower et al. One of ordinary skill in the art would have been motivated to do for the benefit of introducing labeled nucleotides into the nucleic acid molecule for detection.

Regarding claims 17 and 21, the order of combination as described in claims 17 and 21 is not critical to the claimed invention. *In re Burhans*, 69 USPQ 330 states that a selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results.

8. Applicant traverses the rejections on the following grounds: Applicant argues that the subject invention does not require the removal of label after each extension step. Applicant argues that on the other hand, Dower et al. discuss a sequencing scheme that requires removal of label after each extension cycle. Applicant states that as the removal step is an important feature of the Dower et al. method, and it would clearly not have been obvious to modify the teaching of Dower et al. so as to remove the label as does the presently claimed invention. Applicant further argues that consistent with the removal of label after each extension cycle in Dower et al., a further difference between the present invention and Dower et al. is that Dower requires the presence of a blocking agent to ensure that no more than one label becomes incorporated at a given state of primer extension. Applicant argues that such extensive discussion of Dower et al. illustrates that, by employment of a blocking groups, Dower et al. intend to ensure that no more than one label is incorporated in each cycle of primer extension. Applicant finally concludes that all teachings and suggestions in Dower et al. would have taught away from the subject invention.

Art Unit: 1655

9. The arguments have been reviewed but not found persuasive for the reasons that follows: As noted earlier, the open language of the subject invention suggest other method steps and reagents as being encompassed in the instant invention. Therefore, the fact that Dower et al. teaches the use of a blocking groups and removal of labels in one their embodiments is encompassed in the instant invention as written. Furthermore, the claims as broadly written do not suggest that the sequencing method of the instant invention avoids removal of labels and the use of a blocking agent or limits the claims in such a way that the claimed method would not operate as Applicant argues. As stated previously, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In view of the foregoing, the prior art rejections under 35 U.S.C. 103(a) are maintained.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

Art Unit: 1655

calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

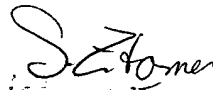
11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The Examiner can normally be reached on Monday through Thursday from 7:00 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Exr.'s supervisor, W. Gary Jones, can be reached at (703) 308-1152. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed the Group's receptionist whose telephone number is (703) 308-0196.

Cynthia B. Wilder, Ph.D.

August 3, 2001


STEPHEN J. JONES
Patent Examiner, Group 1